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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,402	11/03/2003	Jean-Louis Escary	60711.000025	2689

21967 7590 12/29/2005

HUNTON & WILLIAMS LLP
INTELLECTUAL PROPERTY DEPARTMENT
1900 K STREET, N.W.
SUITE 1200
WASHINGTON, DC 20006-1109

EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/698,402	ESCARY, JEAN-LOUIS	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) *1-38,48-52 and 54-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-47 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/13/04 & 3/11/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Appendix A & B1-2*.

DETAILED ACTION

1. Applicant's election with traverse of Group 3 (claims 39-47 and 53) drawn to polypeptides encoded by single nucleotide polymorphisms (SNPs) and therapeutic agents comprising polypeptides encoded by SNPs. Applicants have provisionally elected Group J, drawn to g798c SNP also with traverse. Applicants have also provisionally with traverse elected Group O, drawn to polypeptides encoded by SNPs leading to the amino acid change C122S in the reply filed on 9/29/2005. The traversal is on the ground(s) that there is no search burden on the Office because of the overlapping subject matter and class/subclass. This is not found to be persuasive because nucleotide sequence comprising Group 1 and each amino acid sequence comprising Groups 3 and 4 (including antibodies directed to the polypeptides) is a unique sequence requiring a unique search of the prior art. Polynucleotides listed in Groups 1 are composed of different nucleic acids, suggesting that each encodes a different polypeptide. Further, each polypeptide listed in Groups 3 and 4 is different and is composed of different amino acids, suggesting that each is different polypeptide with diverse functional and structural features. Searching all of the sequences in a single patent application would provide an undue search burden on the Examiner and the USPTO's resources because of the non-coextensive nature of these searches. Applicant has not provided evidence to demonstrate that the polynucleotide and polypeptide sequences are patentably *indistinct* from one another. Therefore, the Examiner has deemed the polynucleotides of Group 1 and the polypeptides of Groups 3 and 4 are independent and distinct inventions,

each from one another. Furthermore, Applicants assert that because several groups (e.g. Groups 5 and 6) share the same class/subclass that they contain overlapping subject matter and that it would not be a serious search burden on the Office. This is not found to be persuasive because although the groups are classified in the same class and subclass, they are directed to different methods steps that require different searches, thus providing an undue search burden on the Examiner and the USPTO.

Further, with respect to Applicants assertion that restriction between the various SNPs of the interferon nucleotide is inappropriate because they share the same utility and share substantial structural feature is not found to be persuasive because changes made at the 11 positions will result in 11 different nucleotide sequences. This will require 11 different searches, thus creating a search burden for the examiner and the Office. Furthermore, with respect to Applicants assertion that restriction between the various SNPs of the interferon polypeptide are inappropriate because they share the same utility and share substantial structural feature is not found to be persuasive because changes made at the 3 amino acid positions will result in 3 different polypeptide sequences. This will require 3 different searches, thus creating a search burden for the examiner and the Office. In addition, claim 53 will be examined to the extent that reads on the instant invention (ex. Polypeptide of SEQ ID NO: 2 and C122S SNP). The requirement is still deemed proper and is therefore made FINAL. Thus claim 39-47 and 53 (in part) will be examined.

Priority

2. Applicant is reminded that in order for a patent issuing on the instant application to obtain the benefit of priority based on priority papers filed in parent Application No. PCT/EP02/05458 filed 5/2/2002, which claims the benefit of French Patent Application No. 01/05919, filed May 03, 2001 under 35 U.S.C. 119(a)-(d) or (f), a claim for such foreign priority must be timely made in this application. To satisfy the requirement of 37 CFR 1.55(a)(2) for a certified copy of the foreign application, applicant may simply identify the application containing the certified copy.

Oath/Declaration

3. Applicant has not signed the instant oath/declaration. It was not executed in accordance with either 37 CFR 1.66 or 1.68.

Drawings

4. The drawings submitted on 11/03/03 is acknowledged.

Information Disclosure Statement

5. The IDS filed 1/13/2004 and 3/11/2004 have been considered.

Specification

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Objections

7. Claim 53 is objected to because of the following informalities: Claim 53 contains subject matter not elected by the Applicant. Claim 53 needs rewritten

limiting the reference to the polypeptide of SEQ ID NO: 2. Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8a. Claims 39-47 and 53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses Q28R, Q70E and C122S of SEQ ID NO: 2 (interferon-α5) substitutions at wild-type positions generate SNPs. This meets the written description of 35 USC 112, first paragraph. However, the specification does not disclose all possible variants (resulting in amino acid residue changes generating 90% -99% homology) of interferon-α5. Applicants have claimed a genus of polypeptides that have no common function (interferon-α5 has antiviral effects and anti tumoral activity etc.). It is not clear what substitutions will retain common functions. Furthermore, the specification fails to disclose if a polypeptide with 90-99% homology containing SNPs Q28R, Q70E and C122S of SEQ ID NO: 2 will be functionally similar to wild type containing the SNP. The specification also fails to disclose the mature and the immature forms of the polypeptide and

the biological activity conferred by such a polypeptide of the instant invention. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of SEQ ID number and the percent identity required. There is not even identification of any particular portion of the structure that must be conserved. The claims as written, however, encompass interferon-α5 variant sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 39-47 and 53. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*See Vas-Cath* at page 1116).

With the exception of isolated interferon-α5 polypeptide with substitutions for example, at wild-type positions Q28R, Q70E and C122S of SEQ ID NO: 2 the skilled artisan cannot envision all the detailed chemical structure of the claimed

polypeptides (with up to 90% identity), regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only the isolated interferon-α5 polypeptide with substitutions at wild-type positions Q28R, Q70E and C122S of SEQ ID NO: 2 but not the full breadth of the claims (with all possible amino acids changed) meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. As a result, it does not appear that the inventors were in possession of various polypeptide sequences set forth in claims 39-47 and 53.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

8b. Claims 39-47 and 53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an interferon-α5 variant, with substitutions such as C122S of SEQ ID NO: 2 of the wild type protein which has

antiviral activity (see Figure 3 of the specification), the disclosure does not reasonably provide enablement for all variants of interferon-α5 (up to 90%) contemplated and which have any and all interferon-α5 type activities.. In addition, it is also unclear what activity if any will be associated or retained with the specific interferon-α5 variants including the mature and the immature forms. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Despite knowledge in the art for producing variants of a given polypeptide with amino acid deletions, insertions or substitutions the specification fails to provide any guidance regarding the changes/modifications contemplated and yet retain the function(s) of the interferon-α5 variants claimed. Furthermore, detailed

information regarding the structural and functional requirements of the disclosed variant protein is lacking. Although it is accepted that the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a protein's structure and function from mere sequence data remains an elusive task. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active variants, this is

not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The instant disclosure fails to disclose which if any functions of the interferon-α5 activities will remain or required after the mutation of the polypeptide. It is also unclear what are functions that will be enhanced following the glycosylation of interferon-α5. Therefore, predicting which variants would retain the functions of the protein is well outside the realm of routine experimentation. Thus, undue amount of experimentation would be required to generate changes/modifications contemplated and yet retain the function of the proteins claimed.

Applicants have not taught how one of skill in the art would use the full scope of polypeptide sequences encompassed by the invention of claims 39-47 and 53. The specification as filed does not sufficiently teach one of skill in the art how to make and/or use the full scope of the claimed sequences. The amount of experimentation required to make and/or use the full scope of the claimed sequences would require trial and error experimentation to determine the functional sequences. Given the breadth of claims 39-47 and 53 in light of the unpredictability of the art as determined by the lack of working examples and

shown by the prior at of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

8c. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39-47 and 53 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39, 42, 45 and 53 are rejected are rejected as being vague and indefinite in the recitation of the term "equivalent position". It is unclear if this means the same SNP change at a different position of SEQ ID NO: 2. Claims 40, 41, 43, 44, 46 and 47 are rejected insofar as they depend on rejected claim 39, 42 and 45.

Claim 53 is rejected are rejected as being vague and indefinite in the recitation of the term "substantially the same biological activity as the mature and immature form". It is unclear if this means the activity is same or within a range. It is also unclear what activity is contemplated by the instant invention. Further, it is not clear what the mature or immature forms of the polypeptide encompass.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

9a. Claim 39-47 and 53 are rejected under 35 U.S.C. 102 (a) or (e) as being anticipated by Chen et al. (U. S. Patent No. 6, 299, 877).

The instant invention is drawn to polypeptide of SEQ ID NO: 2 and therapeutic compounds comprising the polypeptide.

Chen et al. disclose the polypeptide of SEQ ID NO: 2 of the instant invention as SEQ ID NO: 11 (see Appendix A). Thus, it will also anticipate 90% - 99% homology of the sequences contemplated in the instant invention. Biological activity is conferred by the sequence of the polypeptide.In addition, therapeutic agents are also contemplated in the reference (column 8, lines 47-65). Thus,

claims 39-47 and 53 are anticipated by Chen et al. (U. S. Patent No. 6, 299, 877).

9b. Claim 39-47 and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Henco et al. (Accession No. P01569, 1985, ref. 6 of PTO1449 submitted 1/13/2004) or Henco et al (J. Mol. Biol. (1985) ref. 4 of PTO1449 submitted 1/13/2004).

The instant invention is drawn to polypeptide of SEQ ID NO: 2 and therapeutic compounds comprising the polypeptide.

Henco et al. disclose the polypeptide of SEQ ID NO: 2 of the instant invention (see Appendix B1-2). Thus, it will also anticipate 90% -99% homology of the sequences and the biological activity is inherent to the sequence. Since the therapeutic agent (claim 53) comprises the polypeptide of the instant invention, the Henco references anticipates claim 53. Thus, claims 39-47 and 53 are anticipated by Henco et al. (Accession No. P01569, 1985, ref. 6 of PTO1449 submitted 1/13/2004) or Henco et al (J. Mol. Biol. (1985) ref. 4 of PTO1449 submitted 1/13/2004).

10. No claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone

number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS 12/05

ROBERT S. LANDSMAN, PH.D.
PRIMARY EXAMINER

Appendix A Applicant copy

GenCore version 5.1.6
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OM protein - protein search, using sw model

Run on: December 15, 2005, 12:49:43 ; Search time 47 Seconds
(without alignments)
332.462 Million cell updates/sec

Title: US-10-698-402-2
Perfect score: 978
Sequence: 1 MALPFVLLMALVVLNCKSIC.....EIMRSFSLSANLQERLRRKE 189

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 572060 seqs, 82675679 residues

Total number of hits satisfying chosen parameters: 572060

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

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1: /cgn2_6/ptodata/1/iaa/5_COMB.pep:*
2: /cgn2_6/ptodata/1/iaa/6_COMB.pep:*
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6: /cgn2_6/ptodata/1/iaa/backfiles1.pep:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	978	100.0	189	2	US-09-206-935-11	Sequence 11, Appl
2	978	100.0	189	2	US-09-949-016-8554	Sequence 8554, Ap
3	971	99.3	189	1	US-08-026-758-7	Sequence 7, Appli
4	969	99.1	189	2	US-09-206-936-11	Sequence 11, Appl
5	933	95.4	189	1	US-08-026-758-19	Sequence 19, Appl
6	868	88.8	189	2	US-09-949-016-9682	Sequence 9682, Ap
7	868	88.8	189	2	US-09-949-016-9683	Sequence 9683, Ap
8	868	88.8	189	2	US-09-949-016-9684	Sequence 9684, Ap
9	855	87.4	189	1	US-08-026-758-1	Sequence 1, Appli
10	852	87.1	189	2	US-07-145-002B-24	Sequence 24, Appl
11	852	87.1	189	2	US-06-256-204C-24	Sequence 24, Appl
12	851	87.0	189	2	US-09-206-935-19	Sequence 19, Appl
13	851	87.0	189	2	US-09-206-936-19	Sequence 19, Appl
14	851	87.0	189	2	US-07-145-002B-12	Sequence 12, Appl
15	851	87.0	189	2	US-07-145-002B-16	Sequence 16, Appl
16	851	87.0	189	2	US-07-145-002B-22	Sequence 22, Appl
17	851	87.0	189	2	US-06-256-204C-12	Sequence 12, Appl
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19	851	87.0	189	2	US-06-256-204C-22	Sequence 22, Appl
20	851	87.0	189	2	US-09-919-497-73	Sequence 73, Appl
21	846	86.5	189	2	US-07-145-002B-36	Sequence 36, Appl
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24	845	86.4	189	2	US-09-206-936-16	Sequence 16, Appl
25	845	86.4	189	2	US-07-145-002B-28	Sequence 28, Appl
26	845	86.4	189	2	US-06-256-204C-28	Sequence 28, Appl
27	842	86.1	189	1	US-08-026-758-17	Sequence 17, Appl
28	839	85.8	189	1	US-08-026-758-8	Sequence 8, Appli
29	838	85.7	189	2	US-09-206-935-12	Sequence 12, Appl
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31	838	85.7	189	2	US-09-949-016-8553	Sequence 8553, Ap
32	832	85.1	189	2	US-09-206-935-10	Sequence 10, Appl
33	832	85.1	189	2	US-09-206-936-10	Sequence 10, Appl
34	832	85.1	189	2	US-07-145-002B-8	Sequence 8, Appli
35	832	85.1	189	2	US-07-145-002B-20	Sequence 20, Appl
36	832	85.1	189	2	US-06-256-204C-8	Sequence 8, Appli
37	832	85.1	189	2	US-06-256-204C-20	Sequence 20, Appl
38	831	85.0	189	1	US-08-026-758-6	Sequence 6, Appli
39	828	84.7	189	2	US-09-206-935-8	Sequence 8, Appli
40	828	84.7	189	2	US-09-206-936-8	Sequence 8, Appli
41	825	84.4	189	1	US-08-026-758-3	Sequence 3, Appli
42	824	84.3	189	2	US-09-889-035-3	Sequence 3, Appli
43	823	84.2	189	1	US-08-026-758-11	Sequence 11, Appl
44	821	83.9	189	1	US-08-026-758-2	Sequence 2, Appli
45	821	83.9	189	1	US-08-026-758-20	Sequence 20, Appl

ALIGNMENTS

RESULT 1
US-09-206-935-11
; Sequence 11, Application US/09206935
; Patent No. 6299877
; GENERAL INFORMATION:
; APPLICANT: Chen, Jian
; APPLICANT: Godowski, Paul
; APPLICANT: Wood, William I.
; APPLICANT: Zhang, Dong-Xiao
; TITLE OF INVENTION: NOVEL TYPE I INTERFERONS
; FILE REFERENCE: 11669.50US05
; CURRENT APPLICATION NUMBER: US/09/206,935
; CURRENT FILING DATE: 1998-12-07
; EARLIER APPLICATION NUMBER: 60/084,045
; EARLIER FILING DATE: 1998-05-04
; NUMBER OF SEQ ID NOS: 24
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 11
; LENGTH: 189
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-206-935-11

Query Match 100.0%; Score 978; DB 2; Length 189;
Best Local Similarity 100.0%; Pred. No. 1.4e-104;
Matches 189; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MALPFVLLMALVVLNCKSICSLGCDLPQTHSLSNRRTLMIMAQMGRISPFSCLKDRHDFG 60

Qy         61 FPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWDETLLDKFYTELYQQLNDLE 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 FPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWDETLLDKFYTELYQQLNDLE 120

Qy        121 ACMMQEVGVEDTPLMNVDSILTVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSLSAN 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 ACMMQEVGVEDTPLMNVDSILTVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSLSAN 180

Qy        181 LQERLRRKE 189
              |||||||||
Db        181 LQERLRRKE 189
```

RESULT 2
US-09-949-016-8554
; Sequence 8554, Application US/09949016
; Patent No. 6812339
; GENERAL INFORMATION:
; APPLICANT: VENTER, J. Craig et al.

GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: December 15, 2005, 12:49:23 ; Search time 230 Seconds
(without alignments)
579.760 Million cell updates/sec

Title: US-10-698-402-2
Perfect score: 978
Sequence: 1 MALPFVLLMALVVLNCKSIC.....EIMRSFSLSANLQERLRRKE 189

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 2166443 seqs, 705528306 residues

Total number of hits satisfying chosen parameters: 2166443

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : UniProt_05.80:*
1: uniprot_sprot:*
2: uniprot_trembl:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	978	100.0	189	1	IFNA5_HUMAN	P01569 homo sapien
2	978	100.0	189	2	Q52LX3_HUMAN	Q52lx3 homo sapien
3	853	87.2	189	1	IFN21_HUMAN	P01568 homo sapien
4	853	87.2	189	2	Q5VWD1_HUMAN	Q5vwd1 homo sapien
5	845	86.4	189	1	IFN14_HUMAN	P01570 homo sapien
6	845	86.4	189	2	Q5VZ56_HUMAN	Q5vz56 homo sapien
7	838	85.7	189	1	IFNA6_HUMAN	P05013 homo sapien
8	838	85.7	189	2	Q5VYQ1_HUMAN	Q5vyq1 homo sapien
9	832	85.1	189	2	Q52LB8_HUMAN	Q52lb8 homo sapien
10	830	84.9	189	1	IFNA4_HUMAN	P05014 homo sapien
11	830	84.9	189	2	Q5VV15_HUMAN	Q5vv15 homo sapien
12	829	84.8	181	2	Q14608_HUMAN	Q14608 homo sapien
13	828	84.7	189	1	IFNA1_HUMAN	P01562 homo sapien
14	828	84.7	189	2	Q5VYQ2_HUMAN	Q5vyq2 homo sapien
15	821	83.9	189	1	IFN17_HUMAN	P01571 homo sapien
16	821	83.9	189	2	Q5VZ53_HUMAN	Q5vz53 homo sapien
17	820	83.8	189	1	IFN10_HUMAN	P01566 homo sapien
18	820	83.8	189	2	Q5VV13_HUMAN	Q5vv13 homo sapien
19	811	82.9	189	2	Q95J78_SAGOE	Q95j78 saguinus oe
20	809.5	82.8	188	2	Q6DJX8_HUMAN	Q6djx8 homo sapien
21	806.5	82.5	188	1	IFNA2_HUMAN	P01563 homo sapien
22	805	82.3	189	1	IFN16_HUMAN	P05015 homo sapien
23	805	82.3	189	2	Q5VV12_HUMAN	Q5vv12 homo sapien
24	795	81.3	189	1	IFNA7_HUMAN	P01567 homo sapien
25	795	81.3	189	2	Q5VV14_HUMAN	Q5vv14 homo sapien
26	794	81.2	189	2	Q14618_HUMAN	Q14618 homo sapien
27	792	81.0	189	2	Q95J77_SAGOE	Q95j77 saguinus oe
28	778	79.6	189	1	IFNA8_HUMAN	P32881 homo sapien
29	778	79.6	189	2	Q5VYQ3_HUMAN	Q5vyq3 homo sapien
30	773	79.0	174	2	Q8MJT1_SAISC	Q8mjt1 saimiri sci
31	742	75.9	184	1	IFNA4_HORSE	P05006 equus cabal
32	738	75.5	184	1	IFNA2_HORSE	P05004 equus cabal
33	736	75.3	184	1	IFNA1_HORSE	P05003 equus cabal
34	730	74.6	184	1	IFNA3_HORSE	P05005 equus cabal
35	728.5	74.5	166	2	Q86UP4_HUMAN	Q86up4 homo sapien
36	728	74.4	166	2	Q8WZ68_HUMAN	Q8wz68 homo sapien
37	674.5	69.0	154	2	Q6QNB6_HUMAN	Q6qnb6 homo sapien
38	670	68.5	189	1	IFNA1_PIG	P49879 sus scrofa
39	667	68.2	189	2	Q6VAB8_PIG	Q6vab8 sus scrofa
40	640	65.4	189	2	Q68IQ5_PIG	Q68iq5 sus scrofa
41	628	64.2	189	2	Q6QTF5_PIG	Q6qtf5 sus scrofa
42	625	63.9	189	1	IFNAB_BOVIN	P05008 bos taurus
43	624	63.8	189	1	IFNA1_BOVIN	P07348 bos taurus
44	624	63.8	189	1	IFNAH_BOVIN	P49878 bos taurus
45	619	63.3	166	2	Q5U8T2_PIG	Q5u8t2 sus scrofa

ALIGNMENTS

RESULT 1
IFNA5_HUMAN
ID IFNA5_HUMAN STANDARD; PRT; 189 AA.
AC P01569;
DT 21-JUL-1986 (Rel. 01, Created)
DT 13-AUG-1987 (Rel. 05, Last sequence update)
DT 10-MAY-2005 (Rel. 47, Last annotation update)
DE Interferon alpha-5 precursor (Interferon alpha-G) (LeIF G) (Interferon
DE alpha-61).
GN Name=IFNA5;
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae;
OC Homo.
OX NCBI_TaxID=9606;
RN [1]
RP NUCLEOTIDE SEQUENCE.
RX MEDLINE=86037205; PubMed=4057246;
RA Henco K., Brosius J., Fujisawa A., Fujisawa J.-I., Haynes J.R.,
RA Hochstadt J., Kovacic T., Pasek M., Schamboeck A., Schmid J.,
RA Todokoro K., Waelchli M., Nagata S., Weissmann C.;
RT "Structural relationship of human interferon alpha genes and
RT pseudogenes.";
RL J. Mol. Biol. 185:227-260(1985).
RN [2]
RP NUCLEOTIDE SEQUENCE [LARGE SCALE GENOMIC DNA].
RX PubMed=15164053; DOI=10.1038/nature02465;
RA Humphray S.J., Oliver K., Hunt A.R., Plumb R.W., Loveland J.E.,
RA Howe K.L., Andrews T.D., Searle S., Hunt S.E., Scott C.E., Jones M.C.,
RA Ainscough R., Almeida J.P., Ambrose K.D., Ashwell R.I.S.,
RA Babbage A.K., Babbage S., Bagguley C.L., Bailey J., Banerjee R.,
RA Barker D.J., Barlow K.F., Bates K., Beasley H., Beasley O., Bird C.P.,
RA Bray-Allen S., Brown A.J., Brown J.Y., Burford D., Burrill W.,
RA Burton J., Carder C., Carter N.P., Chapman J.C., Chen Y., Clarke G.,
RA Clark S.Y., Clee C.M., Clegg S., Collier R.E., Corby N., Crosier M.,
RA Cummings A.T., Davies J., Dhami P., Dunn M., Dutta I., Dyer L.W.,
RA Earthrowl M.E., Faulkner L., Fleming C.J., Frankish A.,
RA Frankland J.A., French L., Fricker D.G., Garner P., Garnett J.,
RA Ghori J., Gilbert J.G.R., Glison C., Grafham D.V., Gribble S.,
RA Griffiths C., Griffiths-Jones S., Grocock R., Guy J., Hall R.E.,
RA Hammond S., Harley J.L., Harrison E.S.I., Hart E.A., Heath P.D.,
RA Henderson C.D., Hopkins B.L., Howard P.J., Howden P.J., Huckle E.,
RA Johnson C., Johnson D., Joy A.A., Kay M., Keenan S., Kershaw J.K.,
RA Kimberley A.M., King A., Knights A., Laird G.K., Langford C.,
RA Lawlor S., Leongamornlert D.A., Leversha M., Lloyd C., Lloyd D.M.,
RA Lovell J., Martin S., Mashreghi-Mohammadi M., Matthews L., McLaren S.,
RA McLay K.E., McMurray A., Milne S., Nickerson T., Nisbett J.,
RA Nordsiek G., Pearce A.V., Peck A.I., Porter K.M., Pandian R.,
RA Pelan S., Phillimore B., Povey S., Ramsey Y., Rand V., Scharfe M.,
RA Sehra H.K., Shownkeen R., Sims S.K., Skuce C.D., Smith M.,
RA Steward C.A., Swarbreck D., Sycamore N., Tester J., Thorpe A.,
RA Tracey A., Tromans A., Thomas D.W., Wall M., Wallis J.M., West A.P.,
RA Whitehead S.L., Willey D.L., Williams S.A., Wilming L., Wray P.W.,
RA Young L., Ashurst J.L., Coulson A., Blocker H., Durbin R.,

```
RA   Sulston J.E., Hubbard T., Jackson M.J., Bentley D.R., Beck S.,
RA   Rogers J., Dunham I.;
RT   "DNA sequence and analysis of human chromosome 9.";
RL   Nature 429:369-374(2004).
RN   [3]
RP   NUCLEOTIDE SEQUENCE OF 57-189.
RC   TISSUE=Spleen;
RX   MEDLINE=81148795; PubMed=6163083;
RA   Goeddel D.V., Leung D.W., Dull T.J., Gross M., Lawn R.M.,
RA   McCandliss R., Seeburg P.H., Ullrich A., Yelverton E., Gray P.W.;
RT   "The structure of eight distinct cloned human leukocyte interferon
RT   cDNAs.";
RL   Nature 290:20-26(1981).
RN   [4]
RP   PROTEIN SEQUENCE OF 22-36.
RX   PubMed=15340161; DOI=10.1110/ps.04682504;
RA   Zhang Z., Henzel W.J.;
RT   "Signal peptide prediction based on analysis of experimentally
RT   verified cleavage sites.";
RL   Protein Sci. 13:2819-2824(2004).
CC   -!- FUNCTION: Produced by macrophages, IFN-alpha have antiviral
CC       activities. Interferon stimulates the production of two enzymes: a
CC       protein kinase and an oligoadenylate synthetase.
CC   -!- SUBCELLULAR LOCATION: Secreted.
CC   -!- SIMILARITY: Belongs to the alpha/beta interferon family.
CC   ----------------------------------------------------------------------
CC   This Swiss-Prot entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use as long as its content is in no way modified and this statement is not
CC   removed.
CC   ----------------------------------------------------------------------
DR   EMBL; X02956; CAA26702.1; -; Genomic_DNA.
DR   EMBL; AL162420; CAH73189.1; -; Genomic_DNA.
DR   EMBL; V00541; CAA23802.1; -; mRNA.
DR   PIR; S43716; IVHUA7.
DR   HSSP; P01563; 1ITF.
DR   SMR; P01569; 24-189.
DR   Ensembl; ENSG00000147873; Homo sapiens.
DR   HGNC; HGNC:5426; IFNA5.
DR   MIM; 147565; -.
DR   GO; GO:0005126; F:hematopoietin/interferon-class (D200-domain. . .; TAS.
DR   InterPro; IPR000471; Interferon_abd.
DR   PANTHER; PTHR11691; Interferon_abd; 1.
DR   Pfam; PF00143; Interferon; 1.
DR   PRINTS; PR00266; INTERFERONAB.
DR   ProDom; PD000550; Interferon_abd; 1.
DR   PROSITE; PS00252; INTERFERON_A_B_D; 1.
KW   Antiviral defense; Cytokine; Direct protein sequencing;
KW   Multigene family; Signal.
FT   SIGNAL        1     21
FT   CHAIN        22    189       Interferon alpha-5.
FT   DISULFID     24    122       By similarity.
FT   DISULFID     52    162       By similarity.
SQ   SEQUENCE   189 AA;  21942 MW;  C605992FE2E78043 CRC64;

  Query Match             100.0%;  Score 978;  DB 1;  Length 189;
  Best Local Similarity   100.0%;  Pred. No. 1.1e-76;
  Matches  189;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MALPFVLLMALVVLNCKSICSLGCDLPQTHSLSNRRTLMIMAQMGRISPFSCLKDRHDFG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MALPFVLLMALVVLNCKSICSLGCDLPQTHSLSNRRTLMIMAQMGRISPFSCLKDRHDFG 60

Qy         61 FPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWDETLLDKFYTELYQQLNDLE 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        121 ACMMQEVGVEDTPLMNVDSILTVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSLSAN 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 ACMMQEVGVEDTPLMNVDSILTVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSLSAN 180

Qy        181 LQERLRRKE 189
              |||||||||
Db        181 LQERLRRKE 189


RESULT 2
Q52LX3_HUMAN
ID   Q52LX3_HUMAN PRELIMINARY;      PRT;   189 AA.
AC   Q52LX3;
DT   13-SEP-2005 (TrEMBLrel. 31, Created)
DT   13-SEP-2005 (TrEMBLrel. 31, Last sequence update)
DT   13-SEP-2005 (TrEMBLrel. 31, Last annotation update)
DE   Interferon, alpha 5.
GN   Name=IFNA5;
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae;
OC   Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   NUCLEOTIDE SEQUENCE.
RC   TISSUE=Brain;
RX   MEDLINE=22388257; PubMed=12477932; DOI=10.1073/pnas.242603899;
RA   Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA   Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA   Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA   Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA   Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA   Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA   Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA   Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA   Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA   Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA   Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA   Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA   Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA   Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA   Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA   Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
RA   Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
RT   "Generation and initial analysis of more than 15,000 full-length human
RT   and mouse cDNA sequences.";
RL   Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RN   [2]
RP   NUCLEOTIDE SEQUENCE.
RC   TISSUE=Brain;
RG   NIH MGC Project;
RL   Submitted (APR-2005) to the EMBL/GenBank/DDBJ databases.
CC   -!- SUBCELLULAR LOCATION: Secreted (By similarity).
DR   EMBL; BC093757; AAH93757.1; -; mRNA.
DR   EMBL; BC093755; AAH93755.1; -; mRNA.
DR   GO; GO:0005576; C:extracellular region; IEA.
DR   GO; GO:0005126; F:hematopoietin/interferon-class (D200-domain. . .; IEA.
DR   GO; GO:0006952; P:defense response; IEA.
KW   Antiviral defense; Cytokine.
SQ   SEQUENCE   189 AA;  21942 MW;  C605992FE2E78043 CRC64;

  Query Match             100.0%;  Score 978;  DB 2;  Length 189;
  Best Local Similarity   100.0%;  Pred. No. 1.1e-76;
  Matches  189;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MALPFVLLMALVVLNCKSICSLGCDLPQTHSLSNRRTLMIMAQMGRISPFSCLKDRHDFG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MALPFVLLMALVVLNCKSICSLGCDLPQTHSLSNRRTLMIMAQMGRISPFSCLKDRHDFG 60

Qy         61 FPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWDETLLDKFYTELYQQLNDLE 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 FPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWDETLLDKFYTELYQQLNDLE 120

Qy        121 ACMMQEVGVEDTPLMNVDSILTVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSLSAN 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 ACMMQEVGVEDTPLMNVDSILTVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSLSAN 180

Qy        181 LQERLRRKE 189
              |||||||||
Db        181 LQERLRRKE 189
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